

AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph at the first line of the specification as follows:

This application is the national phase under 35 U.S.C. § 371 of PCT International Application No. PCT/JP99/00638 which has an International filing date of February 15, 1999, which designated the United States of America, and this application claims priority of Application No. 050137/1998 filed in Japan on February 15, 1998 under 35 U.S.C. § 119.

Please amend the paragraph starting at page 1, line 25 and ending at page 3, line 7 of the present specification as follows:

The number of patients suffering from these diseases has slightly increased year by year but no effective remedies or prophylaxis have been found ("Immunodeficiency due to medicament", Men-eki Kagaku (Immunological Science), Vol. 9. p.285-289 (1984) Ed. by Yuichi Yamamura, Chuzo Kishimoto, Robert A. Good). Currently, for treatment of these diseases, there have been employed pharmacotherapy including administration of Salazopyrin® ~~Salazopyrin~~, 5-aminosalicylic acid, azathioprine, 6-MP, tranilast, methotrexate, cyclosporine A, or metronidazole, and administration of an excess amount of 7S-immunoglobulin; surgical therapy such as thymectomy or replacement with artificial joint; or symptomatic

therapy such as nutritional therapy (Yoichi Ichikawa et al. "Study on efficacy of long-term administration of methotrexate and salazosulfapyridine on rheumatoid arthritis case" Rheumatism, Vol. 35, p.663-670, (1995); Sadao Kashiwazaki, "Study on efficacy of combination of auranofin and methotrexate on rheumatoid arthritis", Rheumatism, Vol. 36, p.528-544, (1996); Takefumi Furutani et al., "Detrimental event in therapy with low dose methotrexate on rheumatoid arthritis", Rheumatism, Vol. 36, p.746-752, (1996); Nobuo Watanabe, "Pharmacotherapy on juvenile rheumatoid arthritis", Rheumatism, Vol. 36, p.670-675, (1996); Takayasu Yakura, "Immunosuppressive therapy: Treatment of autoimmune diseases", Sogo Rinsho, Vol. 30, p.3358, (1981); Shin Totokawa et al., "Study on methotrexate therapy in rheumatoid arthritis: Seeking for strategy of more effective administration", Rheumatism, Vol. 37, p.681-687 (1997)). However, these therapies are not eradicated but rather are disadvantageous in that they may cause severe adverse side effects due to long-term ingestion of medicaments. Thus, it is desired to develop more effective prophylactics/remedies and therapy.

Please amend the paragraph at page 25, lines 14-25 of the present specification as follows (please note that the recitations of "E. coli" are intended to be underlined as shown in the originally filed specification):

SEB modifications were expressed with modification genes inserted into pTrc99A vector. E. coli cells with the gene incorporated were cultured in culture medium in which 4% ~~CIRCLEGROW®~~ CIRCLEGROW (BIO IOI Inc., Vista, CA, U.S.A.) and ampicillin (50 mg/ml) were dissolved at 37°C for 18 hours. The cells were collected and then suspended in the same medium to 0.3-1.0 of O.D. 550 nm. Thereto was added 2 mM isopropyl-B-D(-)-thiogalactopyranoside (IPTG) and expression was induced by shaking the mixture at 37°C overnight. After induction, the host E. coli cells were removed by centrifugation and supernatant was filtered through 0.45 µm filter membrane.

Please amend the paragraph at page 26, lines 1-10 of the present specification as follows:

The thus prepared supernatant was passed through Sepharose® ~~Sepharose~~ 4B column to which anti-SEB monoclonal antibody SA58-2-6IgG was immobilized so that SEB modifications in the supernatant were adsorbed. The column was washed with 0.1 M Tris HCl (pH 8.0) and then eluted with 4M MgCl₂. The eluted fractions were dialyzed against 20-fold volume of physiological saline three times and then against 20-fold volume of PBS twice. All the SEB modifications prepared herein could be purified with the above monoclonal antibody column.